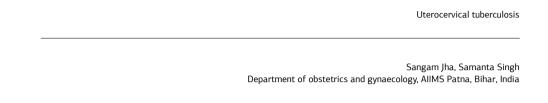
Uterocervical tuberculosis at extremes of reproductive age: A report of two cases



Abstract

Female genital tuberculosis accounts for 9% of all extrapulmonary tuberculosis and one of the major causes of female infertility. Though cervical tuberculosis is rare, an abnormal looking cervix should raise suspicion especially in endemic areas. Here, we report two cases of uterocervical tuberculosis with variable presentation. The first case is a postmenopausal lady who presented with vaginal discharge with friable ulcerative lesion involving the whole of the ectocervix. She was clinically diagnosed as carcinoma cervix stage 1, but histopathology returned as tuberculosis with positive AFB staining. She responded well to the treatment. The second case is a 24-yearold young woman who presented with secondary amenorrhoea for the last 4 years. She had taken antitubercular treatment (ATT) for 6 months two years back for genital tuberculosis but did not get her menses after completion of course. This time, sonography has revealed hematometra. She underwent hysteroscopic adhesiolysis of cervical stenosis and hematometra drainage. Cervical tissue submitted this time for histology came negative for TB. This case report emphasizes the importance of accurate diagnosis and adequate treatment of tuberculosis to avoid complication. Keywords

Genital tuberculosis; Antitubercular treatment (ATT); Hematometra; Cervical stenosis

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Introduction

Tuberculosis is a major public health problem worldwide. Genital tuberculosis is identified as an important cause of female infertility. While lung is thought to be the most commonly affected organ, tuberculosis can affect any organ in the human body. Genitourinary tuberculosis accounts for 27% of extrapulmonary tuberculosis (EPTB) with genital TB being seen in 9% of cases [1]. Clinical presentation of genital tuberculosis is protean in nature and ranges from being asymptomatic to menstrual irregularity and infertility. Cervical tuberculosis can sometimes imitate the symptomatology of cervical cancer. Genital tuberculosis is commonly associated with intrauterine adhesions resulting in amenorrhoea, but the persistence of cervical adhesion leading to hematometra formation after antituberculous treatment is rare. Here we present two cases of genital tuberculosis at extremes of reproductive age with variable presentation.

Case Report

Case 1

A 45-year-old, G5P5 postmenopausal woman presented with the complaints of foul-smelling vaginal discharge for the last 3 months. There was no history of prolonged fever, cough, weight loss or postcoital bleeding. There was no history of contact with TB patient, her previous menstrual cycles were normal. On speculum examination, irregular, friable lesion was seen covering almost the whole of ectocervix which was bleeding when touching (Figure 1). Anteverted, bulky uterus with restricted mobility and bilateral free parametrium was noted on digital examination. Rectal mucosa was free. Clinical diagnosis of carcinoma cervix stage1 was made, hence tissue from the lesion was sent for histopathological examination (HPE). Histology revealed tubercles with granulomatous epithelioid cells and caseation with focal dense neutrophil infiltrates (Figure 2). Zeil Nelson stain for acid-fast bacilli was positive. Her blood picture showed anemia with lymphocytosis and raised ESR. To find out the primary source of infection, examination of sputum for acid-fast bacilli and a chest x-ray was done, but the report came negative, only the Mantoux test was strongly positive. After confirmation of diagnosis, she was put on four drugs isoniazid, rifampicin, ethambutol, and pyrazinamide for two- month intensive phase and isoniazid and rifampicin for four -month continuation phase. After completion of the full course of ATT, cervical lesion healed up and reverted back to a normal look.

Case 2

A 24-year-old woman presented with complaints of amenorrhoea for the last 4 years. She attained menarche at 15 years of age and had regular menstrual flow utill she developed amenorrhoea. There was no history of galactorrhoea. She had a significant past medical history of genital tuberculosis diagnosed on the basis of secondary amenorrhoea and cervical biopsy two years earlier for which she received 6 months of antitubercular treatment. Then her hormonal profile was within normal limits as per her age and ultrasound pelvis revealed the uterus of 6.4x3.3x3 cm size with normal echotexture, the endometrium was 5.4mm thick and cervix was normal in size and echo pattern. Past surgical history was important for illustration, as she was

planned for hysteroscopy and endometrial biopsy for workup of secondary amenorrhoea two years ago but as cervical os could not be identified, only cervical biopsy was taken and sent for histopathological examination. Histopathology reported granulomatous inflammation consistent with tuberculosis. She had completed six months of ATT course but did not resume her menstruation in the following one year, therefore she had been referred to our hospital for further management. She was five feet two inches tall, weighed 54 kg, with welldeveloped secondary sexual characteristics and thyroid was not palpable. The abdomen was soft, no lump was palpable. On gentle speculum examination, the cervix was hypertrophied, but os could not be visualized. Per vaginal examination revealed a boggy mass in posterior fornix, uterus could not be felt separately, bilateral fornices were free. Ultrasonography showed hematometra of 6.01x2.9x3.19 cm size (Figure 3A). After preoperative workup, hysteroscopic resection of cervical obstruction (Figure 3B) followed by hematometra drainage was performed. Cervical and endometrial tissues were sent for histopathological examination. Histopathology of cervical tissue reported no granuloma or malignancy hence considered free of disease. Repeat hysteroscopy had been performed after two months and showed normal uterocervical canal and ostia. She has resumed her normal menstruation 3 months posttreatment.



Figure 1. Naked eye view of the cervix prior to treatment

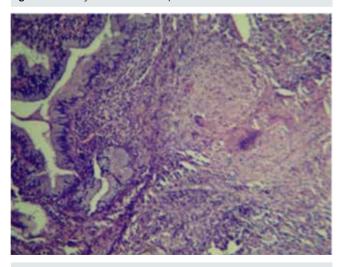


Figure 2. Tubercles with granulomatous epithelioid cells and caseation with focal dense neutrophil infiltrates

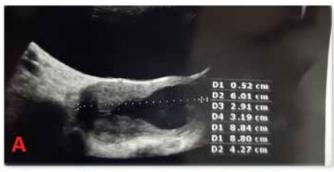




Figure 3. A: Sonographic picture showing hematometra of 6.01x2.9x3.19 cm size. B: Hysteroscopic view of the cervix with fibrosed external os

Discussion

Female genital tuberculosis (FGTB) is most commonly caused by mycobacterium tuberculosis in developing countries. In 95% of genital tuberculosis, cervix is not involved and overall it accounts for 0.1 to 0.65% of all tuberculosis cases [1]. A reduction in cervical immunity status or trauma can promote infection despite the resistance of squamous epithelium of ectocervix. Genital tract is involved from the primary focus, usually lungs, through hematogenous or lymphatic routes, though the primary lesion is healed and non-detectable at the time of presentation. Rarely primary infection of cervix can occur through sexual transmission [2].

Genital tuberculosis can present with menstrual irregularity, postcoital bleeding, vaginal discharge or infertility along with constitutional symptoms. In postmenopausal women, symptomatology can mimic cervical cancer. There could be contact history with the affected individual, but most of the time it is absent as in our both cases. Macroscopic appearance of the tuberculitic cervix can be papillary, ulcerative, interstitial, miliary, endocervical or polypoidal [3,4]. One of our index cases had friable ulcerative growth on the cervix mimicking carcinoma cervix.

As per the WHO definition of EPTB, diagnosis of EPTB should be made on the basis of one culture-positive specimen, or positive histology or strong clinical evidence consistent with active EPTB. Approximately one-third of cases are culture negative [5], as the infecting organism is scanty in genital TB or cyclical shedding leads to inadequate granuloma formation in the endometrium. To maximize the yield in HPE, a specimen should be collected from multiple sites. In one of the two index cases, acid-fast bacilli could be demonstrated in cervical tissue, but in another case with secondary amenorrhoea, diagnosis was based on the presence of typical epitheloid granuloma suggestive of tuberculosis. Newer modalities like GeneXpert can aid in the

faster diagnosis as well as asses rifampicin resistance status which helps in selecting appropriate antitubercular drugs.

Treatment of genital tuberculosis is similar to the TB of other organs. The WHO treatment guidelines for TB (2010) recommend that patients newly diagnosed with TB should receive a regimen containing rifampicin (R) for six months: intensive phase with isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) for two months followed by a continuation phase with HR for four months. Both of our patients were given two-month HRZE and four-month HR. Both of them responded well. Cervical appearance became normal after the completion of ATT. In our second case, endometrium responded well to the treatment as evidenced by endometrial collection but cervix remained fibrosed. She had to undergo adhesiolysis of the endocervical canal in the second sitting for the hematometra drainage. This time cervical tissue submitted for histology and AFB staining returned negative, so considered cured of the disease. Similar cases of genital tuberculosis resulting in secondary amenorrhoea have been reported in the literature [4,6] but no prior case had cervical canal stenosis and required adhesiolysis for hematometra drainage and thus deserve mention.

Fertility outcome after the treatment depends on the severity of the disease at the time of institution of ATT as severe adhesion may persist after treatment. The spontaneous conception rate may vary from 31 to 59% among women treated for FGTB with the better rate among those who were diagnosed and treated earlier. As the fertility outcome is poor even after treatment, primary prevention by minimizing exposure to mycobacteria by adopting respiratory hygiene and safe sexual practice, decrease the disease burden.

Conclusion

Genital tuberculosis can present with nonspecific clinical symptoms. There should be a high index of suspicion of tuberculosis in women with secondary amenorrhoea or an unhealthy cervix, especially in endemic areas. Early diagnosis and timely treatment are vital to avoid complication and restore fertility.

${\bf Scientific} \ {\bf Responsibility} \ {\bf Statement}$

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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